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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,933	03/07/2001	Brett C. Bookser	030727.0042.CIP1	3455

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Jessica R. Wolff, Esq.
Brobeck, Phleger & Harrison LLP
12390 El Camino Real
San Diego, CA 92130-2081

EXAMINER

MCKENZIE, THOMAS C

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 05/14/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/801,933

Applicant(s)

BOOKSER ET AL.

Examiner

Thomas McKenzie Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. This action is in response to an election filed on 3/13/02. There are thirty-six claims pending and thirty-five under consideration. Claims 1-6 and 833 are compound claims. Claims 34-36 are use claims. This is the first action on the merits. The application concerns some phenyl phosphonate compounds and uses thereof. Applicants in their comments correctly pointed out that claim 2 is a linking claim, not a claim drawn exclusively to $R^5 = \text{phenyl}$ compounds. The Examiner made a number of errors in characterizing which claims link which Groups in the restriction. To correct the record the restriction is repeated. This only has a practical effect upon claim 7.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:
- I. Claim 30, drawn to phenyl compounds, compounds of formula I(b) with $X^3-X^5 = \text{carbon}$, classified in class 562, subclass 8, among others.
 - II. Claims none, drawn to pyridine compounds, compounds of formula I(b) with one of $X^3-X^5 = \text{nitrogen}$, classified in class 546, subclass 22, among others.
 - III. Claims none, drawn to thiophene compounds, compounds of formula I(a) with either G^2 or $G^3 = \text{sulfur}$, classified in class 549, subclass 6, among others.
 - IV. Claims none, drawn to furan compounds, compounds of formula I(a) with either G^2 or $G^3 = \text{oxygen}$, classified in class 549, subclass 218, among others.
 - V. Claims none, drawn to oxazoles and thiazoles, compounds of formula I(a) with G^2 or $G^4 = \text{sulfur or oxygen}$ and $G^3 = \text{nitrogen}$, classified in class 548, subclass 119, among others.
 - VI. Claims none, drawn to all other heteroaryl compounds, classified in class 544, subclass 232, among others.

Claim 7 links Groups III-VI.

Claim 8 links Groups I, II, and VI.

Claim 14 links Groups I and II.

Claims 1-6, 9-13, 15-29, and 31-36 link all Groups.

3. Applicant's election with traverse of Group I in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the search would not present a burden to the Examiner. This is not found persuasive because according to the MPEP § “[f]or purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation of separate classification, or separate status in the art, or a different field of search as defined in MPEP § 808.02. That *prima facie* showing may be rebutted by appropriate showings or evidence by the applicant.” The Examiner, in the previous office action, made such a showing of differing classification. Applicants did not rebut this classification analysis.

4. Claim 7 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

5. Claims 1-6, 8-29, and 31-36 are rejected on the grounds as being drawn to an improper Markush group *In re Harnisch* 206 USPQ 300. The claimed compounds, compositions, and methods that employ them present a variable core. Formula (Ia) is drawn to the non-elected inventions. Formula (Ib) contains compounds drawn to the non-elected inventions.

Information Disclosure Statement

6. Applicants IDS (PTO-1449), entered as paper #8 and filed 1/29/02 is noted. However, none of the cited references are presently with the file. A search for the missing references has been initiated.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-17, 19, 26, 30, and 34-36 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase in line 16, page 144 “the cyclic moiety contains a carbonate or thiocarbonate” is indefinite. Does contain mean the functional group forms part of the ring, i.e. a 1,3-dioxane is claimed or is a substituent upon the all carbon ring? If the former, then “alicyclic” is improper because such a ring may not contain any heteroatoms.

If the former, the “carbonate or thiocarbonate” refer to a group of compounds, not the univalent radicals required as substituents.

8. Claims 1-6 and 8-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “prodrugs” occurs repeatedly through the claims. The word “prodrug” is indefinite. The issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' “prodrugs” are molecules whose structure lie outside the subject matter of claim 1, but upon metabolism in the body are converted to active compounds falling within the structural scope of claim 1. The claim describes the function intended but provides no specific structural guidance to what constitutes a “prodrug”. Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

9. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 30 recites the limitation " J^2 etc.

are -OR³" in line 26, page 158. There is no antecedent basis for this limitation in claim 1 which allows J² to be either -R² or -OR¹¹ only.

10. Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a fructose-1,6-bisphosphate dependent disease" is indefinite. The claim provides for the use of the compounds of formula I, but the claims do not set forth any steps involved in determining how to identify "a fructose-1,6-bisphosphate dependent disease". It is unclear what diseases and treatments applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how to practice this use. Identifying which diseases applicants intend this claim to cover will involve extensive and potentially inconclusive clinical research. Without such clinical research to identify the patients and diseases applicants intend to treat, one skilled in the art cannot determine the metes and bounds of the claim. Hence, the claim is indefinite.

11. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "glycogen storage diseases" is indefinite. The phrase is not found in Stedman's Medical Dictionary. The "excess glycogen storage diseases" are mentioned but not defined in lines 1-2, page 4 of the specification. Is this a distinct disease from that Applicants claim? What diseases are being claimed?

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 8-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Determining if a particular substance is a “prodrug” will involve undue experimentation. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Determining whether a particular compound meets these three criteria in a clinical trial setting passes the threshold of undue experimentation.

13. Claims 34 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of diabetes, does not reasonably provide enablement for treatment of “a fructose-1,6-bisphosphate dependent disease” or “glycogen storage diseases” generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Applicants have not demonstrated nor have they alleged there is any correlation between the *in vitro* assay, whose results are described in Table 3, page 133, and clinical efficacy against any specific disease. Case law is clear on this point. In an unpredictable art, such as diabetes pharmacology, *in vitro* assays may

be used for enablement only if there is a well-established correlation between the assay and clinical efficacy.

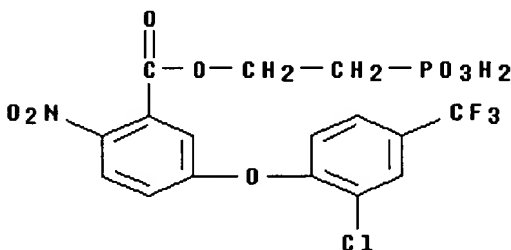
Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 9, 11, 12, 14, 15, 17, 20, 29, are rejected under 35 U.S.C. 102(b) as being anticipated by Diel ('701). There are two compounds taught in this reference that fit formula (I), one of which is shown below. It has both $R^1Y = HO$, $L =$ the alkyleneoxycarbonyl group $-CH_2-CH_2-O-C(O)-$, $R^5 =$ disubstituted phenyl, $J_2 =$ nitro, $J^4 = OR^2$, with $R^2 =$ the substituted aryl group phenyl, where the substituents are the halo group chlorine and the perhaloalkyl group CF_3 . Line 3, page 5 of the specification discloses that all aryl groups may be substituted. The halo group and the perhaloalkyl group are disclosed as permissible substituents in line 26 and line 30 of page 5. The compounds are found in the reference in Table I, column 9 and are compounds 1.03 and 1.16.



Allowable Subject Matter

15. Claims 3-6, 10, 13, 16, 18, 21-28, 30-33, and 35 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

16. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for before final amendments is (703) 872-9306. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Mukund J. Shah

**Mukund Shah
Supervisory Patent Examiner
Art Unit 1624**

TCMcK
May 10, 2002

